

# Effect of intravenous iron in alleviating symptoms of exhaustion in non-anaemic pre-menopausal women

<b>Submission date</b>	<b>Recruitment status</b>	<input type="checkbox"/> Prospectively registered
14/02/2010	No longer recruiting	<input type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
17/03/2010	Completed	<input checked="" type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
30/06/2011	Nutritional, Metabolic, Endocrine	

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

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## Additional identifiers

### Protocol serial number

N/A

## Study information

### Scientific Title

# Effect of intravenous iron versus placebo on exhaustion symptoms in non-anaemic premenopausal women with low ferritin levels

## Acronym

FERRIM

## Study objectives

Administration of intravenous iron to non-anemic pre-menopausal women with low serum ferritin (S-ferritin) levels will improve physical and mental performance

Please note that as of 24/05/10 a brief description of the study results has been added to this record. More details are available in the interventions section below.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Both local and central ethical approval was obtained prior to study start - study conducted according to Swissmedic, ICH GCP guidelines and Declaration of Helsinki

## Study design

Randomised multicentre double blind placebo controlled superiority study

## Primary study design

Interventional

## Study type(s)

Treatment

## Health condition(s) or problem(s) studied

Reduced physical and mental performance in pre-menopausal women

## Interventions

Venofer®, (iron sucrose injection) is an aqueous complex of polynuclear iron (III)- hydroxide in sucrose for intravenous use. Patients received either 2 infusions each containing 200 mg iron [III]-hydroxide sucrose (Venofer®) or 2 infusions of 200 ml 0.9% saline (placebo) administered over a minimum period of 10 minutes each week for the first two weeks of the trial. Each patient received a total of 4 infusions representing a total of 800 mg of iron in the Venofer® treated group. Patients were followed for total period of 3 months.

Added 24/05/10:

Statistical methods:

For description of the distribution medians and range were used. For analysis of differences of distribution of investigated parameters between Venofer and placebo groups, a non parametric test (Mann- Whitney U-Test) was used. Both types of analyses were performed, because deviations from normal distribution were found for primary objective variables, most items are categorically scaled parameters.

## Study Results:

### 1. Efficacy:

Difference from baseline in median Brief Fatigue Inventory (BFI) score between the treatment

groups was not statistically significant but suggest a trend toward a greater improvement in patients treated with iron sucrose (difference in change BFI: -0.44, p=0.076). There was a significantly (p=0.036) greater improvement in categorized tBFI scores from baseline to Day 42 in patients treated with IV iron sucrose compared to patients treated with placebo. There were significant differences between the study groups in some sub-group analyses. Among patients presenting with severe iron deficiency at baseline (defined as TSAT below 20% and serum ferritin below 50 ng/mL or serum ferritin below 15 ng/mL) there was a significantly greater improvement in BFI score at Day 42, in patients treated with IV iron sucrose compared to patients treated with placebo (p=0.026).

There was a significant correlation between the change in fatigue from baseline to Day 42 as measured by the BFI and the change in fatigue as measured by Short Performance Inventory (SPI), a global investigator assessment ( $r=0.59$ ,  $p<0.0001$ ).

Patients treated with IV iron sucrose showed a significant increase in serum-ferritin values during the study compared to baseline, and this increase was significantly greater in the IV iron sucrose group compared to the placebo group ( $p<0.0001$ ).

The results of this study suggest a clinical benefit for patients treated with iron sucrose and warrant further investigation in this area.

## 2. Safety:

In total, 54 of 89 enrolled patients reported at least one adverse effect (AE) during the clinical study; most of the AEs were mild and unrelated to study medication. Two serious AEs (SAEs) were reported, one in each treatment group. There was one case of appendicitis and one serious traffic accident. Both were unrelated to treatment. Further, there were no clinically relevant abnormal findings in vital signs, physical exams or evaluation of concomitant medication during the study. This suggests that the iron sucrose treatment caused no safety concerns. It can be concluded that the incidence of AEs following iron sucrose administration is low and reflects the safety profile labelled in the SmPC.

### **Intervention Type**

Drug

### **Phase**

Not Specified

### **Drug/device/biological/vaccine name(s)**

Iron [III]-hydroxide sucrose (Venofer®)

### **Primary outcome(s)**

1. Brief Fatigue Inventory (total score = tBFI) assessed at baseline, day 42 and 90
2. Serum ferretin, assessed at baseline, 3rd treatment visit, day 42 and 90

### **Key secondary outcome(s)**

1. BFI intensity mean score and impairment score, assessed at baseline, day 42 and 90
2. Haematological parameters, assessed at baseline, day 42 and 90
  - 2.1. Hb
  - 2.2. Mean corpuscular volume (MCV)
  - 2.3. Mean corpuscular haemoglobin concentration (MCHC)
  - 2.4. Haematocrit (HCT)
3. Iron status, assessed at baseline, 3rd treatment visit, day 42 and 90
  - 3.1. Serum iron
  - 3.2. Transferrin Saturation (Tsat)

3.3. Transferrin

4. Safety

4.1. Adverse effects

4.2. Physical exam, assessed at day 90

4.3. Body weight and height, assessed at day 90

4.4. Vital signs, assessed at baseline, day 42 and 90

4.5. Creatinine, assessed at baseline

4.6. Alanine Aminotransferase (ALT), assessed at baseline

4.7. Aspartate Aminotransferase (AST), assessed at baseline

4.8. C-Reactive protein (CRP), assessed at baseline, day 42 and 90

5. Concomitant medications

#### **Completion date**

07/08/2008

## **Eligibility**

#### **Key inclusion criteria**

1. Premenopausal, regularly menstruating women
2. Age  $\geq$  18 years
3. S-ferretin  $< 50\text{ng/mL}$
4. Signed informed consent
5. Reduced physical and mental performance (fatigue, depressive mood, dizziness, sleep disturbance, concentration, neck pain, headache) as determined by investigator
6. Adequate contraception

#### **Participant type(s)**

Patient

#### **Healthy volunteers allowed**

No

#### **Age group**

Adult

#### **Lower age limit**

18 years

#### **Sex**

Female

#### **Key exclusion criteria**

1. Haemoglobin (Hb) level 120 g/L
2. Known mental and physical disorder (cancer, depression)
3. Use of concomitant medication to cause symptoms of fatigue and depression (antidepressive & chemotherapeutic agents, sedatives)
4. Use of iron preparations within previous 4-weeks
5. Active severe infection, inflammation, malignancy
6. C-Reactive Protein (CRP)  $> 20\text{ mg/mL}$
7. Thyroid-Stimulating Hormone (TSH)  $> 4\text{ micro U/mL}$

8. Use of menstruation depressing gestagens
9. History of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV)
10. Significant cardiovascular disease e.g. unstable angina, New York Heart Association (NYHA) class IV
11. Hypersensitivity to iron sucrose or iron sulphate
12. Pregnancy or lactation
13. Participation in any other therapeutic study in the previous month

**Date of first enrolment**

21/09/2006

**Date of final enrolment**

07/08/2008

## Locations

**Countries of recruitment**

Switzerland

**Study participating centre**  
Gynakologie Geburtshilfe Seefeld  
Zurich  
Switzerland  
CH-8008

## Sponsor information

**Organisation**

Vifor Pharma, Vifor (International) Ltd (Switzerland)

**ROR**

<https://ror.org/0185z7g17>

## Funder(s)

**Funder type**

Industry

**Funder Name**

Vifor Pharma, Vifor (International) Ltd. (Switzerland)

# Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	22/09/2011		Yes	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes